WE CLAIM:

1. A reverse genetics system for screening and identifying antiflaviviral compounds.

2. A reverse genetics system for screening and identifying attenuated flaviviral vaccines.

3. The reverse genetics system according to claims 1 and 2 comprising a full-length lineage I WNV cDNA clone.

4. The reverse genetics system according to claims 1 and 2 comprising a lineage I WNV replicon.

5. The reverse genetics system of claim 3, wherein the full-length lineage I WNV cDNA comprises a promoter sequence operably linked to the WNV cDNA and a first nucleotide sequence encoding a first reporter.

6. The reverse genetics system of claim 4, wherein the lineage I WNV replicon comprises a promoter sequence operably linked to the WNV replicon and a first nucleotide sequence encoding a first reporter.

7. The reverse genetics system of claims 5 and 6, wherein the first nucleotide sequence encoding a reporter is selected from the group consisting of a nucleotide sequence encoding a luciferase reporter, a green fluorescent protein reporter, beta-galactosidase, an oxidase, a peptidase, a glycosidase, a phosphatase, a fluorescent protein reporter, and an antibiotic resistance marker.

8. The reverse genetics system of claim 5, wherein the WNV cDNA further comprises a second nucleotide sequence encoding a second reporter.

9. The reverse genetics system of claim 6, wherein the WNV replicon further comprises a second nucleotide sequence encoding a second reporter.

10. The reverse genetics systems of claims 8 and 9, wherein the second reporter is a selectable marker.

11. The reverse genetics systems of claim 10, wherein the selectable marker is neomycin-resistance marker (Neo).

12. The reverse genetics systems of claims 6 and 9, wherein the first nucleotide sequence encoding the first reporter is a nucleotide sequence encoding green fluorescent protein and the second nucleotide sequence encoding the second reporter is a neomycin resistance marker.

13. The reverse genetics system of claims 5 and 6, wherein the promoter is selected from the group consisting of a prokaryotic promoter, a eukaryotic promoter, and a viral promoter.

14. The reverse genetics system of claim 13, wherein the viral promoter is selected from the group consisting of SP6, T7, and T3.

15. The reverse genetics system of claims 5 and 6, wherein the nucleotide sequence encoding a reporter further comprises an internal ribosome entry site (IRES) to control translation of said reporter.

16. A recombinant plasmid comprising the reverse genetics system of claim 5.

17. A recombinant plasmid comprising the reverse genetics system of claim 6.

18. A method for preparing a fully-infectious RNA transcript from the reverse genetics system of claim 5, comprising the step of contacting the reverse genetics system with an DNA-dependent RNA polymerase that recognizes the promoter sequence operably linked to the WNV cDNA under conditions sufficient for transcription to occur.

19. A method for preparing a cell line stably replicating the reverse genetics system of claim 11 comprising the steps of:

(a) transfecting a cell host with the reverse genetics system of claim 11,

(b) selecting for cells resistant to neomycin.

20. A cell line stably replicating the reverse genetics system of claim 11.

21. A cell line stably replicating the reverse genetics system of claim 12.

22. The method of preparing the cell line of claim 19, wherein the cell host is capable of being infected by and supporting the replication of a flavivirus.

23. The method of preparing the cell line of claim 22, wherein the flavivirus is selected from the group consisting of WNV, DENV, JEV, SLEV, and YFV.

24. The method of preparing the cell line of claim 19, wherein the cell host is an animal cell.

25. The method of preparing the cell line of claim 19, wherein the animal cell is a mammalian cell.

26. The method of preparing the cell line of claim 24, wherein the mammalian cell is BHK-21.

27. The method of preparing the cell line of claim 24, wherein the mammalian cell is a Vero cell (ATCC CCL-81).

28. The reverse genetics system of claim 8, wherein the first nucleotide sequence encoding a reporter and second nucleotide sequence encoding a reporter are joined in the same reading frame and are together preceded by an IRES, wherein said IRES directs the translation of the first and second reporters.

29. The reverse system of claim 9, wherein the first nucleotide sequence encoding a reporter and second nucleotide sequence encoding a reporter are translationally fused and are preceded by an IRES, wherein said IRES directs the translation of the first and second reporters.

30. The reverse genetics systems of claims 28 and 29, wherein the first nucleotide sequence encoding a reporter and second nucleotide sequence encoding a reporter are linked by an autoprotease nucleotide sequence.

31. The reverse genetics systems of claim 30, wherein the autoprotease nucleotide sequence is a foot and mouth disease virus 2a autoprotease nucleotide sequence.

32. A recombinant plasmid containing a cDNA sequence corresponding to WNV lineage I, wherein said recombinant plasmid further comprises a promoter sequence adapted to control cDNA transcription and at least one nucleotide sequence encoding a reporter, wherein said reporter indicates the level of transcription of said cDNA sequence corresponding to WNV lineage I.

33. A method of identifying potential antiflaviral chemotherapeutics comprising the steps of:

(a) contacting the cell line of claim 20 with a potential chemotherapeutic compound,

(b) measuring the level of expression of said first reporter,

wherein a reduced expression level of said first reporter indicates a potential antiflaviviral chemotherapeutic.

34. A method of collecting and transmitting a dataset comprising the steps of:

(a) carrying out the method of claim 33 to provide a dataset,

(b) collecting and storing said dataset,

(c) transmitting said dataset.

35. The method of collecting and transmitting a dataset of claim 34, wherein step (c) occurs electronically.

36. The method of collecting and transmitting a dataset of claim 34, wherein step (c) occurs by email.

37. The method of collecting and transmitting a dataset of claim 34, wherein step (c) occurs by posting on a network.

38. The method of collecting and transmitting a dataset of claim 37, wherein the network is a global communications network.

39. A pharmaceutical composition comprising the antiflaviral chemotherapeutic of claim 33.

40. A method for administering the pharmaceutical compostion of claim 39 to a subject infected with a flavivirus, comprising the step of administering the pharmaceutical composition in a therapeutically effective amount.

41. A method for generating a potential attenuated WNV vaccine comprising the steps of:
(a) mutating a sequence in the reverse genetics system of claim 5 to provide a mutated reverse genetics system,
(b) transforming a host cell with the mutated reverse genetics system,
(c) detecting a decrease in the reporter expression,
wherein detecting a decrease in reporter gene expression indicates a potential attenuated WNV vaccine.

42. The method for generating an attenuated WNV vaccine of claim 41 further comprising the step of measuring the virulence of the potential attenuated WNV vaccine.

43. A method of a generating live-attenuated WNV lineage I virus vaccine comprising the steps of:

(a) deleting portions of a regulatory sequence located at the 3' end of a lineage I WNV cDNA clone comprising at least one nucleotide sequence encoding a reporter to provide a modified lineage I WNV cDNA clone,

(b) transforming a suitable host cell line with said modified lineage I WNV cDNA clone,

(c) measuring the expression level of said reporter,

wherein a low expression level of said reporter may indicate a live-attenuated WNV lineage I virus vaccine.

44. A method of treating a flaviviral infection comprising the steps of:

(a) identifying an antiflaviviral chemotherapeutic drug by the method of claim 33,

(b) administering the antiflaviviral chemotherapeutic in a therapeutic effective amount,

wherein in the therapeutic effective amount of the antiflaviviral chemotherapeutic treats the flaviviral infection.

45. A DNA molecule comprising a DNA sequence encoding a mRNA of a lineage I WNV genome, said DNA sequence having a 5' and a 3' end, said DNA molecule adapted to report the transcription of said DNA sequence, said DNA molecule comprising:

(a) a deletion in said DNA sequence corresponding to one or more structural genes of said lineage I WNV genome;

(b) a promoter at said 5' end of said DNA sequence;

(c) a nucleotide sequence encoding a reporter at said 3' end of the DNA sequence;

wherein said promoter is operably linked and adapted to control the transcription of said DNA sequence and said nucleotide sequence encoding said reporter.

46. The DNA molecule according to claim 45, wherein said lineage I WNV genome is according to SEQ ID NO.2.

47. The DNA molecule according to claim 45, wherein said reporter is selected from the group consisting of luciferase, green fluorescent protein, beta-glactosidase, oxidase, peptidase, glycosidase, phosphatase, a fluorescent protein, and an antibiotic resistance marker.

48. The DNA molecule according to claim 45, where said reporter is green fluorescent protein.

49. The DNA molecule according to claim 45, wherein said reporter is luciferase.

50. The DNA molecule according to claim 45, wherein said one or more structural genes is selected from the group consisiting of the capsid, envelope, and membrane genes.

51. The DNA molecule according to claim 45, wherein said deletion is in the capsid, envelope, and membrane genes of said lineage I WNV genome.

52. The DNA molecule according to claim 45, wherein said reporter is a selectable marker.

53. The DNA molecule according to claim 52, wherein said selectable marker is a neomycin resistance marker (Neo).

54. The DNA molecule according to claim 45, wherein said promoter is selected from the group consisting of SP6, T7, and T3.

55. The DNA molecule according to claim 45, wherein said DNA molecule contains a second nucleotide sequence encoding a reporter, wherein transcription of said second nucleotide sequence encoding said second reporter under control of said promoter.

56. The DNA molecule according to claim 55, wherein the second reporter is selected from the group consisting of luciferase, green fluorescent protein, beta-glactosidase, oxidase, peptidase, glycosidase, phosphatase, a fluorescent protein, and an antibiotic resistance marker.

57. The DNA molecule according to claims 55, wherein the first and second nucleotide sequences encoding first and second reporters are optionally preceded by an internal ribosome entry site (IRES), wherein said IRES facilitates translation of said first and second reporters.

58. The DNA molecule according to claim 45, wherein the DNA sequence is a lineage I WNV replicon and said reporter is GFP or luciferase.

59. A DNA molecule comprising a DNA sequence encoding a full-length and fully-infectious mRNA of a lineage I WNV genome, said DNA sequence having a 5' and a 3' end, said DNA molecule adapted to report the transcription of said DNA sequence, said DNA molecule comprising:

(a) a promoter at said 5' end of said DNA sequence;

(b) a first nucleotide sequence encoding a first reporter gene at said 3' end of the DNA sequence;

wherein said promoter is adapted to control the transcription of said DNA sequence and said reporter gene.

60. The DNA molecule according to claim 59, wherein said lineage I WNV genome is according to SEQ ID NO.2.

61. The DNA molecule according to claim 59, wherein said reporter is selected from the group consisting of luciferase, green fluorescent protein, beta-glactosidase, oxidase, peptidase, glycosidase, phosphatase, a fluorescent protein, and an antibiotic resistance marker.

62. The DNA molecule according to claim 59, where said first reporter is green fluorescent protein.

63. The DNA molecule according to claim 59, wherein said first reporter gene is luciferase.

64. The DNA molecule according to claim 59, wherein said first reporter is a selectable marker.

65. The DNA molecule according to claim 64, wherein said selectable marker is a neomycin resistance marker (Neo).

66. The DNA molecule according to claim 59, wherein said promoter is selected from the group consisting of SP6, T7, and T3.

67. The DNA molecule according to claim 59, wherein said DNA molecule comprises a second nucleotide sequence encoding a second reporter, wherein the transcription of said second nucleotide sequence encoding the second reporter is under control of said promoter.

68. The DNA molecule according to claim 67, wherein the second reporter is selected from the group consisting of luciferase, green fluorescent protein, beta-glactosidase, oxidase, peptidase, glycosidase, phosphatase, a fluorescent protein, and an antibiotic resistance marker.

69. The DNA molecule according to claims 68, wherein the first and second nucleotide sequences encoding said first and second reporters are optionally preceded by an internal ribosome entry site (IRES), wherein said IRES facilitates translation of said first and second reporters.

70. A method for screening a plurality of compounds comprising at least one flavivirus inhibitor to detect and identify said flavivirus inhibitor, wherin said flavivirus inhibitor inhibits a flavivirus, comprising the steps:

(a) providing a cell line comprised of cells each comprising a flavivirus reverse genetics system engineered with a least one nucleotide sequence encoding a reporter adapted to emit a fluorescence signal;

(b) detecting a first fluorescence signal of said cells;

(c) contacting in a reaction well said cells with said plurality of compounds;

(d) incubating the cells to allow said plurality of compounds to penetrate the cells;

(e) detecting a second fluorescence signal of said cells;

(a) comparing the first and second fluorescence signals;

wherein a lower second relative fluorescence signal indicates the presence of a flavivirus inhibitor.

71. The method according to claim 70, wherein the cell line is stable.

72. The method according to claim 70, wherein the method is carried out in a high throughput manner.

73. The method according to claim 70, wherein the reaction well is a well of a multi-well microplate.

74. The method according to claim 70, wherein the cell line is comprised of cells selected from the group consisting of animal, insect, mammalian, and human cells.

75. The method according to claim 70, wherein the cell line is BHK-21.

76. The method according to claim 70, wherein the cell line is Vero.

77. The method according to claim 70, wherein the reporter is selected from the group consisting of luciferase and green fluorescent protein.

78. The method according to claim 77, wherein said assay further comprises the step of storing the first and second relative fluorescence signals in a database.

79. The method according to claim 78, wherein said method further comprises the step of providing access to the database to a third party, wherein said third party analyzes the database to identify the flavivirus inhibitor.

80. A high throughput assay for screening a plurality of compounds comprising at least one flavivirus inhibitor to detect and identify said flavivirus inhibitor, wherin said flavivirus inhibitor inhibits a flavivirus, comprising the steps:

(a) providing a cell line comprising cells each comprising the DNA molecule of claim 45;

(b) detecting a first relative fluorescence signal of said cells;

(c) contacting in a reaction well said cells with said plurality of compounds;

(d) incubating the cells to allow said plurality of compounds to penetrate the cells;

(e) detecting a second relative fluorescence signal of said cells;

(f) comparing the first and second relative fluorescence signals;

wherein a lower second relative fluorescence signal indicates the presence of a flavivirus inhibitor.

81. The high throughput assay according to claim 80, wherein said assay further comprises the step of storing the first and second relative fluorescence signals in a database.

82. The method according to claim 81, wherein said method further comprises the step of providing access to the database to a third party, wherein said third party analyzes the database to identify the flavivirus inhibitor.

83. The method according to claim 80, wherein the cell line is stable.

84. The method according to claim 80, wherein the reaction well is a well of a multi-well microplate.

85. The method according to claim 80, wherein the cell line is comprised of cells selected from the group consisting of animal, insect, mammalian, and human cells.

86. The method according to claim 80, wherein the cell line is BHK-21.

87. The method according to claim 80, wherein the cell line is Vero.

88. The method according to claim 80, wherein the reporter is selected from the group consisting of luciferase and green fluorescent protein.

89. The method according to claim 70, wherein the flavivirus is selected from the group consisting of WNV, DENV-1, DENV-2, DENV-3, DENV-4, JEV, SLEV, YFV, MFEV, AV, KV, JV, CV, YV, and any combination thereof.

90. The high throughput assay according to claim 80, wherein the flavivirus is selected from the group consisting of WNV, DENV-1, DENV-2, DENV-3, DENV-4, JEV, SLEV, YFV, MFEV, AV, KV, JV, CV, YV, and any combination thereof.

91. A composition comprising the flavivirus inhibitor identified by the method according to claim 70.

92. A composition comprising the flavivirus inhibitor identified by the high throughput assay according to claim 80.

93. A cell line comprising the DNA molecule according to claim 45.

94. A cell line comprising the DNA molecule according to claim 59.